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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,577	12/16/2005	Tetsuro Kikuchi	Q86357	6428

23373 7590 06/24/2009
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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,577	KIKUCHI ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,37-41,43-49 and 51-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 37-41, 43-49 and 51-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 37- 41, 43-49 and 51-69 are pending

Amended claims set submitted on 03/18/2009 is acknowledged where claims 37, 44-45, 51-52, 54-56, 60-63 and 67-69 were amended and claims 42 and 50 were cancelled.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/18/2009 has been entered.

Applicants' arguments, filed 03/18/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102(e)

New grounds of rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 37, 41, 43-45, 54-55 and 59--62 are rejected under 35 U.S.C. 102(b), as being anticipated by Migaly (WO 2004/010932, Filing date 25th July 2003 which claims priority to provisional US application dated 30th July 2002) referenced in the instant IDS).

Migaly discloses method of treatment of major depressive disorder by administering a combination of two categories of drugs, antipsychotic in combination with a selective serotonin reuptake inhibitor (abstract, reference claim 1). Migaly discloses that such a combination provides the following benefits: preventing disease progression/modifying the course of depression, delaying/preventing relapse or recurrence of depression, preventing the development of delusional/psychotic depression, being protective/(and/or) remedying the development of tolerance toward the antidepressant, and a possibility for providing a neuroprotective effect and finally it may also provide a more effective treatment, increase the response rate to treatment, treat the residual symptoms of depression, prevent the antidepressant's paradoxical effect of sensitizing patients to depression and relapse, and prevent the worsening of depression caused by the antidepressants. (page 6, lines 7-15). Migaly discloses the method wherein the antipsychotic drug used in the combination is a dopamine system stabilizer such as aripiprazole (reference claims 7-9) and wherein the said antidepressant is selected form the group consisting of serotonin reuptake inhibitors

selected from a group consisting of fluoxetine, , norfluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram, bupropion, nefazodone, mirtazapine , venlafaxine, duloxefine, elomipramine, milnacipran, reboxetine, nisoxetine, zimelidine, litoxetine, indalpine, gepirone, femoxetine and alaproclate (reference claim 14). Migaly specifically discloses the method of his invention wherein the antidepressant is fluoxetine or paroxetine or sertraline or fluvoxamine and the antipsychotic is aripiprazole (reference claims 19, 23, 27 and 31). Migaly discloses dosage forms of the combination which includes capsule, tablets etc preferably for oral administration (page 9, lines 26-31).

With regards to the instant claims 41, 49 and 59 which recites the pharmaceutical combination of the aripiprazole and an antidepressant further comprising a pharmaceutically acceptable carriers, Migaly's disclosure of the combination of drugs in dosage forms, clearly anticipates these claims since pharmaceutical dosage forms consists of the drugs in combination with a pharmaceutically acceptable carrier and other excipients.

Accordingly Claims 1, 37, 41, 43-45, 54-55 and 59--62 are anticipated by Migaly.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 37-39, 41, 43-49, 51-57 and 59-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al(US 2002/0156067, already of record) in view of Winnans (American Journal of Health-system and pharmacy, vol. 60, Dec 1, 2003; page 2437-2447, already of record) further in view of Harvey et al

Wong expressly teaches pharmaceutical composition and methods of their use comprising a) one or more norepinephrine reuptake inhibitors and b) one or more

neuroleptic agents (WONG claim 1). Among the compounds listed for component a) are duloxetine, venlafaxine, and milnacipran (WONG claim 2). These are the identical compounds listed as examples of serotonin reuptake inhibitors useful in the instant application (instant app claims 1, 37, 54 and 55). Among the compounds listed by WONG et al. as neuroleptic agents, component b), is aripiprazole (WONG claim 5). This is the exact compound presented in the instant application (instant app claims 1 and 54). Example 2 (WONG et al.) describes the preparation of the composition, in that the active components are combined in a pharmaceutically acceptable carrier (WONG page 6, column 1, paragraph 47, lines 1-3). Thus anticipating instant application claims 41 and 59. Wong discloses that the composition of his invention is used to treat any of the diseases or disorders of the central nervous system. Representative diseases or disorders include, but are not limited to the following: depression, schizophrenia, neurodegenerative disorders, migraine headaches, cluster headaches, an age-associated learning and mental disorder, bipolar disorder, a movement disorder (e.g., Tourette's syndrome)etc. ([0042] and claims 1,2,5,9 and 19 which are conditions overlapping those specifically recited in instant claims 42-45 and 54-55, 60-62. Wong teaches that both commonly used typical and atypical neuroleptic agents can cause number of neurological side effects [0013-0014]. Wong also teaches the need for a pharmaceutical compositions that would have both the therapeutic benefits of the neuroleptics agents (typical or atypical) but with reduced side effects [0013]. Furthermore Wong teaches that the combination of the norepinephrine reuptake

inhibitor with a neuroleptic provides rapid relief to those suffering from disorders of the central nervous system with a minimal amount of deleterious side effects [0044].

Wong does not specifically teach metabolites of aripiprazole such as dehydroaripiprazole etc. or wherein aripiprazole or the norepinephrine reuptake inhibitor to be specifically escitalopram or citalopram.

Winans teaches the pharmacology, pharmacokinetics, clinical efficacy, adverse effects, drug interactions and dosage of aripiprazole (abstract). Winans teaches that the major metabolite of aripiprazole is dehydro-aripiprazole which has demonstrated similar affinities for D2 receptors and represents approximately 40% of aripiprazole's AUC in the plasma (page 3, left col. 3rd paragraph). Additionally, Winann teaches that when aripiprazole was administered with divalproex moderate change in pharmacokinetic parameters were observed and similar effects were observed when the active metabolite was administered with divalproex (page 7, right col., and 3rd paragraph). As such, the substitution of aripiprazole taught by Wong with its metabolites such as dehydro-aripiprazole would have been *prima facia* obvious to one of ordinary skill in the art because the metabolites are expressly taught in the prior art to have similar activity as the parent drug.

With references to the specific serotonin reuptake inhibitors citalopram and escitalopram claimed in the instant application, these two drugs elicit anti-depressant effect by inhibiting serotonin reuptake. Although Wong is silent as to these specific drugs, Wong cites drugs such as venlafaxine, which also inhibits serotonin reuptake as evidenced by applicants as evidenced by Harvey et al (Arch Gen Psychiatry/ vol 57,

May 2000, page 503-509). Harvey teaches that venlafaxine is an antidepressant with a mechanism of action that is believed to involve inhibition of the uptake pumps for serotonin and norepinephrine (page 503, left col. 1st paragraph) and concludes that the in-vivo evidence in healthy humans suggests that both serotonin (5-HT) and norepinephrine uptake inhibitions are mechanisms of action of venlafaxine. Citalopram and escitalopram are also serotonin reuptake inhibitors as evidenced by Owens (CNS Spectr, abstract, 2002 Apr/ 7 (4) page 34-9). Owens teaches that citalopram is one of a selective serotonin reuptake inhibitor and it's S-enantiomer also known as escitalopram is one of the most selective serotonin reuptake inhibitor available. As such venlafaxine taught by Wong is a functional equivalent of citalopram and escitalopram and thus substitution of the antidepressants taught by Wong with other similarly functioning drugs such as citalopram or escitalopram would have been obvious to one of ordinary skill in the art at the time of invention.

In view of the foregoing references, the instantly claimed pharmaceutical composition would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made. Wong teaches pharmaceutical composition comprising of (a) one or more norepinephrine reuptake inhibitors and (b) one or more neuroleptic agents. Accordingly all of the materials instantly claimed were known in the art to be for treatment of the disorders of the central nervous system. The prior art also teaches solution to the problem of decreasing adverse effects experienced with treatment of neuroleptics alone. This solutions to the prior art problem which is the combination of the neuroleptics with norepinephrine reuptake inhibitors also provides

the skilled artisan motivation to combine the references. An ordinarily skilled artisan will be imbued with at least a reasonable expectation of success that a compositions comprising the serotonin, norepinephrine receptor uptake inhibitors with known neuroleptics will result in the decrease of deleterious effects associated with neuroleptic treatment alone.

Response to applicant's arguments submitted on 03/18/2009

Applicants traverse the above rejection with the following arguments:

a. the examiner has not identified a teaching or suggestion in the prior art which may have served as a motivation for one of ordinary skill in the art to combine the cited references

b. Venlafaxine has dual functions and is therefore not a functional equivalent of escitalopram and citalopram as alleged by the examiner.

c. Unexpectedly superior results as shown in the declaration under 37 C.F.R. 1.132 was obtained with their instant invention.

Applicant's traversal arguments for this rejection have been fully considered, but are not found to be persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re*

Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). It is also noted that "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). In this instance Wong et al provides explicit teachings that the combination of a neuroleptic agent and a norepinephrine reuptake inhibitor are useful in the treatment of diseases or disorders of the central nervous system. Wong provides additional motivation to combine the two drugs since the combination provides rapid relief to the person suffering from these disorders with a minimal amount of deleterious effects. Winans teaches that aripiprazole and dihydro-aripiparzole have similar effects and as such an ordinarily skilled artisan would have ample knowledge from the prior art to utilize either aripiprazole or dihydro-aripiprazole in the combination taught by Wong et al.

In response to applicant's argument that Venlafaxine is not a functional equivalent of Citalopram and escitalopram, while agreeing with the applicant that Venlafaxine may not have properties identical to citalopram and escitalopram, it is art recognized that Venlafaxine has serotonin reuptake inhibition property which is the activity also displayed by citalopram and escitalopram and all three drugs are known

anti-depressants. As such venlafaxine produces the same effects produced by citalopram or escitalopram albeit may not be to the same extent which makes them functional equivalent. . Additionally, it is pointed out that venlafaxine has been categorized as a serotonin reuptake inhibitor along with escitalopram by the applicant (see the 1-132 declaration submitted page 2, under materials and methods).

. With regards to the Applicant's argument of unexpected results, Applicants data presented in the 35 U.S.C 1.132 declaration and the instant specifications has been considered and found not persuasive.

The data disclosed by the applicant in does not include combination of aripiprazole or dehydroaripiprazole with citalopram which is instantly claimed in instant claims 39, 47, 57 and 64. The testing was carried out with very specific parameters such as the dosage of aripiprazole was 0.01 mg/kg and the dosages used for the SRI drugs differed, for e.g. duloxetine, venlafaxine , escitalopram and paroxetine was used at 10 mg/kg, milnacipram was used at 30 mg/kg and sertraline was used at 3 mg/kg. The aripiprazole was injected IP in a specific vehicle which is 0.1% acetic acid-saline followed by oral administration of the SRI in a specific vehicle which is 5% gum arabica-distilled water. As such the two drugs in the combination were administered sequentially by different routes of administration.

Accordingly, the exact dosages of the agents and the sequence of addition is very critical to achieve the effect observed in the study .The instant claims do not recite these limitations required to achieve the unexpected results. For example, instant claim 1 is drawn to a composition comprising the combination of aripiprazole or its metabolite

with any of the listed serotonin reuptake inhibitor which includes citalopram, fluoxetine and fluvoxamine which have not been demonstrated to have unexpected results. The composition also implies a composition comprising both the drugs in a vehicle and not separate drugs in different vehicles. The method claims 54-69, as written implies the administration of the two agents as a combination in a single vehicle through a single route of administration. Therefore, the unexpected results observed in these studies are with very specific parameters and specific drug combinations and are therefore not commensurate with the full scope of what is claimed and the data is not probative of nonobviousness of the full scope of the claims as discussed above.

Accordingly, the arguments set forth by the applicant are unpersuasive and the rejection is maintained.

New grounds of rejection

Claims 1, 37-39, 41, 43-49, 51-57 and 59-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Migaly (WO 2004/010932, referenced in the IDS) in view of Winnans (American Journal of Health-system and pharmacy, vol. 60, Dec 1, 2003; page 2437-2447, already of record).

Migaly discloses method of treatment of major depressive disorder by administering a combination of two categories of drugs, antipsychotic in combination with a selective serotonin reuptake inhibitor (abstract, reference claim 1). Migaly discloses that such a combination provides the following benefits: preventing disease progression/modifying the course of depression, delaying/preventing relapse or recurrence of depression,

preventing the development of delusional/psychotic depression, being protective/(and/or) remedying the development of tolerance toward the antidepressant, and a possibility for providing a neuroprotective effect and finally it may also provide a more effective treatment, increase the response rate to treatment, treat the residual symptoms of depression, prevent the antidepressant's paradoxical effect of sensitizing patients to depression and relapse, and prevent the worsening of depression caused by the antidepressants. (page 6, lines 7-15). Migaly discloses the method wherein the antipsychotic drug used in the combination is a dopamine system stabilizer such as aripiprazole (reference claims 7-9) and wherein the said antidepressant is selected form the group consisting of serotonin reuptake inhibitors selected from a group consisting of fluoxetine, , norfluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram, bupropion, nefazodone, mirtazapine , venlafaxine, duloxefine, elomipramine, milnacipran, reboxetine, nisoxetine, zimelidine, litoxetine, indalpine, gepirone, femoxetine and alaproclate (reference claim 14). Migaly specifically discloses the method of his invention wherein the antidepressant is fluoxetine or paroxetine or sertraline or fluvoxamine and the antipsychotic is aripiprazole (reference claims 19, 23, 27 and 31). Migaly discloses dosage forms of the combination which includes capsule, tablets etc preferably for oral administration (page 9, lines 26-31).

With regards to the instant claims 41, 49 and 59 which recites the pharmaceutical combination of the aripiprazole and an antidepressant further comprising a pharmaceutically acceptable carriers, Migaly's disclosure of the combination of drugs in dosage forms, clearly anticipates these claims since pharmaceutical dosage forms

consists of the drugs in combination with a pharmaceutically acceptable carrier and other excipients.

Migaly does not specifically teach metabolites of aripiprazole such as dehydroaripiprazole etc.

Winans teaches the pharmacology, pharmacokinetics, clinical efficacy, adverse effects, drug interactions and dosage of aripiprazole (abstract). Winans teaches that the major metabolite of aripiprazole is dehydro-aripiprazole which has demonstrated similar affinities for D2 receptors and represents approximately 40% of aripiprazole AUC in the plasma (page 3, left col. 3rd paragraph). Additionally, Winnan teaches that when aripiprazole was administered with divalproex moderate change in pharmacokinetic parameters were observed and similar effects were observed when the active metabolite was administered with divalproex (page 7, right col., and 3rd paragraph). As such, the substitution of aripiprazole taught by Wong with its metabolites such as dehydro-aripiprazole would have been *prima facia* obvious to one of ordinary skill in the art because the metabolites are expressly taught in the prior art to have similar activity as the parent drug.

In view of the foregoing references, the instantly claimed pharmaceutical composition would have been prima facia obvious to one of ordinary skill in the art at the time the invention was mad. Migaly explicitly teaches pharmaceutical composition comprising of (a) antipsychotic agents such as aripiprazole and (b) antidepressants which are serotonin reuptake inhibitors such as those instantly claimed. Accordingly all of the materials instantly claimed were known in the art to be used for treatment of the

depression. Migaly also teaches the benefits of using such a combination of drugs in the treatment of depression which provides an ordinarily skilled artisan motivation to develop a composition comprising a combination of these two agents and a method of treating depression with them. An ordinarily skilled artisan will be imbued with at least a reasonable expectation of success that a compositions comprising the serotonin, norepinephrine receptor uptake inhibitors with aripiprazole will improve the antidepressant effect of the antidepressant alone with added benefits as taught by Migaly.

Claim 40 and 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang and Winnans or Migaly and Winnans as applied to claims 1, 37-39, 41, 43-49, 51-57 and 59-69 above, and further in view of Bando et al (US 2004/0058935, PCT filing date of Sept 25, 2002)

Wang and Winnans or Migaly and Winnans teach as discussed supra and are applied here in the same manner. The cited references do not teach the composition or the method wherein the aripiprazole is anhydrous aripiprazole crystals B.

However, Bando et al teaches low hygroscopic forms of aripiprazole and processes for their preparations thereof which will not convert to a hydrate or lose their original solubility even when a medicinal preparation containing the aripiprazole anhydride crystals is stored for an extended period. (Abstract). Bando et al teaches the disadvantages of using hydrous forms of aripiprazole, (i) the hydrous forms of aripiprazole have the disadvantage of being less bioavailable and less dissoluble than

the anhydrous forms of aripiprazole (ii)the variation in the amount of hydrous versus anhydrous aripiprazole drug substance from batch to batch could fail to meet specifications set by drug regulatory agencies. (iii) The milling may cause the drug substance, conventional anhydride, to adhere to manufacturing equipment which may further result in processing delay, increased operator involvement, increased cost, increased maintenance and lower production yield.(iv) the potential for absorbance of moisture during storage and handling would adversely affect the dissolubility of aripiprazole drug substance. Thus shelf-life of the product could be significantly decreased and/or packaging costs could be significantly increased [0006]. Bando et al teaches a reduced hygroscopic form of aripiprazole which is a crystalline substance defined as Anhydride B which is more amenable to pharmaceutical processing and formulation [0009] According to another embodiment of the fourth aspect of the present invention is provided aripiprazole drug substance of low hygroscopicity wherein said drug substance is aripiprazole Anhydride Crystals B and will not substantially convert to a hydrous form of aripiprazole when properly stored even for an extended period. For instance, said aripiprazole anhydride crystals B can be stored under a relative humidity (RH) of 60% and at a temperature of 25.degree. C., even for a period not less than 4 year [0083]

Therefore, it would have been obvious to one of ordinary skilled in the art to combine the teachings of the cited references above and use aripiprazole B in the compositions and methods taught be Wang and Winnans or Migaly and Winnans. An ordinarily skilled artisan would be motivated from Bando et al's teachings of the

disadvantages of the hydrous aripiprazole and the advantages of using anhydrous crystals of aripiprazole B which in medicinal compositions which is increase in stability and decrease in costs. Bando et al's teachings provide an artisan a reasonable expectation of success that using aripiprazole B in place of other aripiprazole in a composition would enhance its stability and ultimately reduce costs.

Conclusion

Claims 1, 37- 41, 43-49 and 51-69 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614